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ORIGINAL ARTICLE

Echocardiographic evaluation of cardiac functions in newborns of mildly preeclamptic pregnant women within postnatal 24–48 hours

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ABSTRACT

The aim of this study is to detect preeclampsia-related cardiac dysfunction within 24–48 hours of delivery in newborns born from preeclamptic mothers. Forty newborns from mildly preeclamptic mothers formed the study group and the control group was formed by 40 healthy newborns. Cardiac function for the groups were evaluated using conventional echocardiography and myocardial performance index (MPI) within the first 24–48 hours of their lifetime and the results of both groups were compared. A significant difference between the groups was observed especially in the PW Doppler MPI measurements (the left ventricle MPI 0.37 ± 0.09 and 0.26 ± 0.11, $p < .001$; the right ventricle MPI 0.29 ± 0.08 and 0.26 ± 0.07, $p < .035$) for the control group and the study group. Elongation in the left and right ventricle MPI was detected to be more significant in terms of comparing systolic and diastolic functions to determine preeclampsia-related cardiac injury in newborns from preeclamptic mothers within the first 24–48 hours of their lifetime.

IMPACT STATEMENT

- Today, the methods which may detect cardiac injury earlier than conventional echocardiographic methods are used for evaluating cardiac functions. Among them, myocardial performance index (MPI) measurement with PW Doppler is the most common ones.
- While studies are available in the literature evaluating foetal cardiac functions with MPI in foetuses of preeclamptic women, studies evaluating cardiac functions with MPI index within the first 24–48 hours in postnatal period are not available. This is the first study to detect cardiac injury by measuring cardiac functions of the newborns of preeclamptic babies using conventional echocardiography (EF, SF, mitral and tricuspid E/A) and myocardial performance index within the first 24–48 hours of life and compare these values with those of a control group composed of healthy newborns with similar demographic characteristics.
- According to the results of the study, elongation in right and left ventricle MPI was detected to be more significant compared to systolic and diastolic functions for determining preeclampsia-related cardiac injury in newborns of preeclamptic mothers within 24–48 hours of delivery. Ventricle functions of the newborns of preeclamptic mothers should also be evaluated with MPI measurement besides conventional echocardiographic measurements.

KEYWORDS
Preeclampsia; myocardial performance index; preeclampsia-related cardiac injury; newborn

Introduction

Preeclampsia/eclampsia is one of the most important causes of maternal and foetal morbidity and mortality. Preeclampsia is defined as hypertension developing following inadequate placenta invasion accompanied by proteinuria and it is seen in ~2% of all pregnant women (ACOG 2002). Neonatal complications of preeclampsia include intrauterine growth restriction (IUGR), hypoxia-related neurologic injury, preterm delivery, perinatal death and long-term cardiovascular morbidity associated with low birth weight (Sibai et al. 2005). Foetal and neonatal cardiac dysfunctions and mild myocardial injury occur due to preeclampsia reported in the literature (Aardema et al. 2001; Balli et al. 2013). Nowadays, there are plenty of methods which are able to detect a cardiac injury earlier than conventional echocardiographic methods. Among these methods, MPI measurement with PW Doppler is the most prevalent (ACOG 2002).

Myocardial performance index (MPI) is also defined as 'Tei index'. MPI which is frequently used in adult and paediatric cardiology is an index that may globally evaluate left and right ventricle functions through combining systolic and diastolic time intervals in cardiac cycle. Myocardial performance index is obtained by dividing the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) by ejection time (ET). It was first used by Tei et al. in 1995 (Berzooe and Kheirandish 2004).

While studies are available in literature evaluating foetal cardiac functions with MPI in foetuses of preeclamptic women, studies evaluating cardiac functions with MPI index

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Table 1. Exclusion criteria of the preeclamptic pregnant women and their newborns.

Exclusion criteria of preeclamptic pregnant women	Exclusion criteria of the newborns of preeclamptic pregnant women
Severe preeclampsia	Babies with history of asphyxia during labour
Chronic diseases (renal, vascular, connective tissue diseases, etc.)	Babies who were applied resuscitation requiring positive pressure ventilation during labour
Diabetes mellitus, gestational diabetes	Congenital or chromosomal foetal anomaly
Presence of chronic hypertension before pregnancy	Newborns who do not have an optimal image quality
Multiple pregnancy	Dysmorphic newborn
Pregnant women <20 years or >35 years	Newborns who showed agitation and anxiety, incompliance during the test

within the first 24–48 hours in the postnatal period are not available. Therefore, our study would be the first study published in the literature. In our study, we tried to detect cardiac injury by measuring cardiac functions of newborn preeclamptic mothers by using conventional echocardiography (EF, SF, mitral and tricuspid E/A) and also using myocardial performance index in the first 24–48 hours of their lifetime. We compared these values with those of the control group composed of healthy newborns who have similar demographic characteristics.

Materials and methods

A total of 60 mildly preeclamptic pregnant women who gave birth at Ege Maternity and Research and Training Hospital between May 2012 and February 2014 were included in this study. Forty-seven of the preeclamptic pregnant women met inclusion criteria during their follow-up in pregnancy. Seven of the newborns were excluded from the study in their postnatal period. Consequently, the newborns of 40 mildly preeclamptic pregnant women who met inclusion criteria made up the study group. Other 40 healthy newborns who do not have preeclampsia and who have similar gestational week, weight and gender were included in the control group. Diagnosis of mild preeclampsia was made based on the diagnostic criteria of American College of Obstetricians and Gynecologists (Cunning et al. 2001). Severe preeclampsia criteria are shown as follows:

1. Elevated resting blood pressure measured with minimum 6 hour intervals, systolic BP >160 mmHg, diastolic BP >110 mmHg (no need to wait for 6 hours if diastolic BP is above 110 mmHg)
2. Detection of min 5 gr proteinuria in 24-hour urine or +3 or more proteinuria in two separate urine analysis done with 4-hour interval
3. Anuria, oliguria (less than 500 ml of urine in 24 hours)
4. Pulmonary oedema or cyanosis
5. Cerebral or visual disorders, altered conscious, headache, scotoma, blurred vision
6. Epigastric or right upper quadrant pain due to Glisson capsule tension
7. Impaired liver functions of unknown origin
8. Thrombocytopenia
9. Intrauterine growth retardation

While severe preeclampsia is defined as the presence of one or more of these diagnostic criteria, mild preeclampsia is defined as preeclamptic patients who do not meet these criteria (Cunning et al. 2001). All of the pregnant women who participated in this study were not in severe preeclampsia criteria. Inclusion and exclusion criteria of the study (mildly preeclamptic pregnant women and newborns) and control group are shown in Table 1.

The study was started after local ethics committee's approval had been obtained. Cardiac functions of the patients in study and control groups were evaluated echocardiographically. Two-dimensional, M-mode, PW Doppler, continuous and colour flow Doppler echocardiographic examinations were performed using a Vivid-6 S 256 model device (GE Vingmed Ultrasound AS, Horten, Norway) with three S-MHz transducer according to the recommendations of the American Society of Echocardiography (Eidem et al. 2000). All of the foetal echocardiographic measurements were made by a single experienced paediatric cardiologist (UK) with a calculated intraclass correlation coefficient of 0.824, revealing a high reproducibility ($p = .018$).

Systolic functions of the left ventricle (ejection fraction (EF) and fractional shortening (FS)) were calculated by determining left ventricular end-diastolic diameter (left VEDD) and left ventricular end-systolic diameter (left VESD) with M-mode in parasternal long-axis view, just distal to the tip of the mitral valve leaflets in diastole. Diastolic functions of the left ventricle were calculated by determining mitral peak early filling velocity (E), atrial contraction peak velocity (A) and E/A ratio with PW Doppler in apical four-chamber view.

PW Doppler measurements of time intervals in order to determine left venticular MPI (Tei index) were performed from the time intervals obtained from apical four-chamber and five-chamber view. Time interval from the end of mitral A wave to the onset of mitral E wave was determined as total ventricular systole (a). LV ejection time was determined by measuring systolic ejection flow in a different heart cycle and apical five-chamber view, by positioning sample volume at the far end of valves. Time interval from the onset to the end of this wave was recorded as ejection time (b).

PW Doppler MPI (left V) was calculated as subtracting ventricular ejection time (b) from left ventricular systole time (a) and dividing the remainder by ventricular ejection time (a-b/b). Measurements were performed in at least three consecutive cycles and mean values were determined (Figure 1).

PW Doppler measurements of time intervals in order to determine right ventricular MPI (Tei index) were performed from the time intervals obtained from apical four-chamber and parasternal short axis view. The time interval from the end of tricuspid A wave to the onset of tricuspid E wave was determined as total ventricular systole (a). RV ejection time was determined by measuring systolic ejection flow in a different heart cycle and short axis view with pulmonary valve at wide open position, by positioning sample volume at the

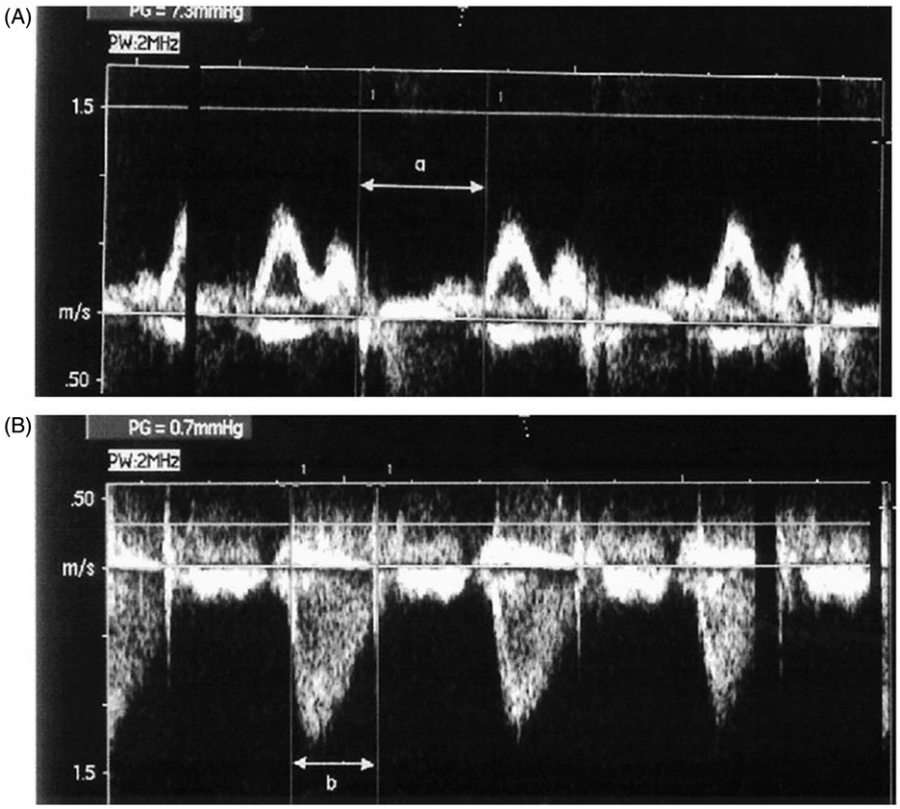

Figure 1. Measurement of time intervals used to calculate left ventricle myocardial performance index by PW Doppler method in different heart cycles: (A) total ventricular systole (a) and (B) left ventricle ejection time (b).

far end of valves. Time interval from the onset to the end of this wave was recorded as ejection time (b). Tei index (right V) was calculated by subtracting ventricular ejection time (b) from left ventricular systole time (a) and dividing the remainder by ventricular ejection time (a–b/b) (Berzooe and Kheirandish 2004). Measurements were performed in at least three consecutive cycles and mean values were determined.

Statistical analysis

SPSS 12.0 (Chicago, IL) for Windows package programme was used for statistical analysis. Kolmogorov–Smirnov test was used for the analysis of distribution of echocardiographic findings of the study group and control group. Student's *t*-test was used for the comparison of numerical data showing normal distribution, and Mann–Whitney's *U*-test was used for the comparison of data not showing normal distribution. The linear correlation between in-group variables was done using the Pearson correlation analysis or Spearman rho analysis. A p level of <0.05 was accepted as statistically significant.

Results

While median age was 26 years (min 21–max 34) in the study group, it was found to be 25 years (min 20–max 35) in the control group. Of a total of 80 patients, 40 comprised the study group (47.5% girls) and 40 comprised the control group (50% girls). Demographic characteristics of both the groups are shown in Table 2. No statistical difference was found between groups with regard to weight, type of delivery, week of delivery and gender ($p > .005$). Left ventricle FS varied between 36% and 43% in the control group (mean 37.07 ± 5.61), and it was found as 31% and 46% in the study group (mean 37.46 ± 4.03) ($p > .05$).

Table 2. Demographic characteristics of study and control group.

	Study group ($n = 40$)	Control group ($n = 40$)	p
Weight (g)	3271 ± 402	3157 ± 196	.113
Caesarean Section (%)	55	45	.371
Gestational week	38.72 ± 0.90	$38.35 \pm 0,80$	.064
Female (%)	47,5	50	.823
Median age	26	25	.433

A statistically significant difference was not detected between the control and study group with regard to conventional echocardiographic measurements (shortening fraction (SF), mitral and tricuspid E/A with pulse wave, peak systolic gradient of aortic and pulmonary flow) of left and right ventricular ($p > .05$) (Tables 3 and 4).

While left ventricle PW Doppler MPI mean was 0.26 ± 0.11 in the control group, it was found 0.37 ± 0.09 in the study group ($p < .001$). While right ventricle PW Doppler MPI mean was 0.26 ± 0.07 in the control group, it was found as 0.29 ± 0.08 in the study group ($p = .035$) (Tables 3 and 4).

While a statistically significant difference was not detected between total systole time (a) of left and right ventricle used for the calculation of MPI of left ventricle (left ventricle a; 24 ± 0.03 and 0.24 ± 0.02, $p > .05$, right ventricle a; 0.25 ± 0.02 and 0.20 ± 0.01, $p < 0.05$), ventricle ejection time was found to be statistically significantly decreased in the study group (left ventricle b; 0.19 ± 0.01 and 0.24 ± 0.02, $p < .001$, right ventricle b; 0.20 ± 0.01 and 0.18 ± 0.01, $p = .027$). In conclusion, the

Table 3. Comparison of left ventricular M-mode, PW Doppler and MPI echocardiographic parameters between study and control groups.

	Study group ($n = 40$)	Control group ($n = 40$)	p
LVEDD (mm)	19.2 ± 1.7	21.3 ± 2.3	.423
EF (%)	70.52 ± 5.13	69.53 ± 3.37	.308
SF (%)	37.46 ± 4.03	37.07 ± 5.61	.724
APV (cm/sec)	1.2 ± 0.21	1.4 ± 0.11	.014
E flow velocity (cm/sec)	0.61 ± 0.21	0.60 ± 0.11	.476
A flow velocity (cm/sec)	0.58 ± 0.17	0.52 ± 0.11	.143
E/A	1.11 ± 0.48	1.16 ± 0.31	.312
a (msn)	0.24 ± 0.02	0.24 ± 0.03	.745
b (msn)	0.18 ± 0.01	0.19 ± 0.01	<.001
MPI	0.37 ± 0.09	0.26 ± 0.11	<.001

EF: ejection fraction; FS: fractional shortening; APV: aortic peak velocity; LVEDD: left ventricular end-diastolic diameter; a: total ventricular systole; b: ventricle ejection time; MPI: myocardial performance index.

Table 4. Comparison of right ventricular echocardiographic data obtained from the study and control groups.

	Study group ($n = 40$)	Control group ($n = 40$)	p
RVEDD (mm)	7.4 ± 2.4	7.6 ± 2.2	.62
PPV (cm/sec)	0.9 ± 0.2	1.2 ± 0.1	.023
E flow velocity (cm/sec)	0.52 ± 0.11	0.52 ± 0.10	.904
A flow velocity (cm/sec)	0.65 ± 0.13	0.60 ± 0.09	.079
E/A	0.81 ± 0.14	0.85 ± 0.24	.201
a (msn)	0.25 ± 0.01	0.25 ± 0.02	.425
b (msn)	0.18 ± 0.01	0.20 ± 0.01	.027
MPI	0.29 ± 0.08	0.26 ± 0.07	.035

a: total ventricular systole; b: ventricle ejection time; PPV: pulmonary peak velocity; RVEDD: right ventricular end-diastolic diameter; MPI: myocardial performance index.

elongation in MPI of right and left ventricle was found to be related with shortening of ventricular ejection time.

Discussion

Preeclampsia is defined as pregnancy-induced hypertension accompanied by proteinuria and seen in 2% of all pregnancies (Eto et al. 1999; Jurko et al. 2011). Pathophysiology of preeclampsia includes abnormal localisation of placenta and inadequate invasion of trophoblasts to spiral arteries of the mother. When trophoblasts do not invade sufficiently, peripheral vascular resistance which should decrease together with advancing gestational week increases and uteroplacental insufficiency develops (Grossman 1991; Harada et al. 1994).

Early onset cardiovascular morbidity of newborn of preeclampsia mother is not sufficiently published in the literature. There are few reports of preeclampsia-related foetal and neonatal cardiac dysfunction and mild myocardial injury in literature (ACOG 2002; Balli et al. 2013). These studies have shown an increase in peripheral vascular resistance which also leads to an increase in afterload of the foetal heart. It causes a decrease in the blood flow of the vital organs such as the brain, the liver and all together it leads to an uteroplacental insufficiency.

Two-dimensional, M-mode and PW Doppler echocardiography is used for the measurement of systolic and diastolic functions of left and right ventricle on conventional echocardiography done for detecting cardiac dysfunction. However, measurement of functions with conventional echocardiography is not reliable due to triangle anatomy of right ventricle and in presence of diseases changing the geometry of left ventricle (Harada et al. 1999). Therefore, using MPI which is frequently used for evaluating cardiac functions in adult and paediatric cardiology, which may measure both systolic and diastolic functions of ventricle and produced from systolic and diastolic time intervals is recommended in recent years (Khong et al. 1986; Harada et al. 2000; Ishii et al. 2000; Api et al. 2009).

MPI is a non-invasive, easily applicable index which has low intraobserver and interobserver differences and it does not take a long time. Intervals are used independently from ventricle geometry, and therefore, it is not affected from blood pressure, heart rate and age. So, it has a high prognostic value for the observation of different clinical entities and it may be used safely (Tei et al. 1995; Narin et al. 1999; Berzooe & Kheirandish 2004).

The value of MPI changes with age. In a study conducted with 161 healthy children aged between 30 days and 18 years, MPI was shown to prolong within the first three years and did not change after 3 years. While normal MPI value is 0.40 ± 0.09 below 3 years, it was reported as 0.33 ± 0.02 after 18 years. It was reported that this change resulted from myocardial maturation and MPI did not change after 3 years, as maturation has been completed (Mori et al. 2004). In another study evaluating normal value of right ventricle MPI in 150 healthy children, right ventricle MPI was detected not to prolong with age and it was found as 0.24 ± 0.04 (Sahn et al. 1978).

Left ventricle MPI was found as 0.32 ± 0.07 and right ventricle MPI was found as 0.27 ± 0.09 in the study of Jurko et al. conducted with healthy children (Tei et al. 1996). Berzooe & Kheirandish (2004). reported right ventricle MPI as 0.25 ± 0.09 and left ventricle MPI as 0.36 ± 0.11 in their study conducted with 108 children (Tsutsumi et al. 2004). In our study, mean right ventricle MPI was found as 0.24 ± 0.07 and left ventricle MPI was found as 0.24 ± 0.11, consistently with literature.

Tsutsumi et al. evaluated 50 healthy newborns just after birth and measured right and left ventricle MPI and reported that MPI temporally prolonged before 24 hours and stayed constant after 24 hours. They associated the temporal prolongation of MPI within the first 24 hours with intrapartum hypoxia (World Health Organization 2005). They concluded that its returning normal thereafter was associated with most of cardiac output's being provided from left ventricle instead of right ventricle as the result of increased pulmonary blood flow due to decreased pulmonary vascular resistance (Khong et al. 1986; World Health Organization 2005). We did not evaluate cardiac functions within the first 24 hours in newborns of preeclamptic pregnant women because we wanted to prevent the hemodynamic changes within the first 24 hours to affect our study.

In literature, we did not encounter a MPI study performed for evaluating preeclampsia-related cardiac injury in newborns of preeclamptic mothers. However, an ample amount of studies are available evaluating cardiac functions in foetal life (Balli et al. 2013, ACOG 2002).

Api et al. allocated the foetuses in three groups in their modified MPI study performed for showing cardiac involvement in mild and severe preeclamptic pregnant women. Group 1 was composed of 72 foetuses of healthy pregnant

women, group 2 was composed of 15 foetuses of mildly preeclamptic mothers, and group 3 was composed of 17 severely preeclamptic mothers. They did not find a statistically significant difference between three groups with regard to MPI change (group 1: 0.43 ± 0.045 and group 2: 0.44 ± 0.064, group 3: 0.44 ± 0.064; $p = .680$). However, they detected a decrease in mitral E, an increase in mitral A and a decrease in aortic flow rate in this study, and they associated with afterload increase in foetal heart due to preeclampsia. The authors reported that cardiac hemodynamic changes could occur due to increased afterload in foetuses of preeclamptic mothers; however, this did not lead to cardiac dysfunction (Api et al. 2009). We detected that MPI prolonged in our study, differently from this literature, and we detected that cardiac hemodynamic changes occurred due to increased afterload, similarly to this literature.

In the study of Balli et al., while a difference was not detected between control and study groups with regard to conventional echocardiographic measurements of foetuses of mildly preeclamptic mothers (EF, SF, MV E/A, TV E/A), they detected that MPI prolonged, pulmonary and aortic peak systolic gradient decreased in the study group. They associated these changes with preeclampsia-related increased afterload and reported that cardiac injury and dysfunction developed due to increased afterload (Balli et al. 2013). The results of our study conducted in newborn period were found to be similar to those of Balli et al. We detected that MPI prolonged, pulmonary and aortic peak systolic gradient decreased in our study.

In our study, decreased pulmonary and aortic peak gradient which are the hemodynamic findings of increased afterload together with prolonged right and left MPI were detected. These results of our study showed that increased peripheral vascular resistance resulting from increased afterload during foetal life stayed the same also on postnatal Day 2 besides preeclampsia-related subclinical cardiac dysfunction in newborns of preeclamptic mothers. Continuing peripheral vascular resistance in postnatal period suggested that vasoactive mediators increased in favour of vasoconstrictive mediators released from the heart and vascular structures in response to increased afterload and increased response to injured endothelium to vasoconstrictive mediators during the preeclamptic pregnancy.

In our study, a significant difference was not detected between systolic and diastolic functions of study and control groups evaluated with conventional echocardiography. We detected that the cause of prolongation of MPI of right and left ventricle arose from the significant shortening in ejection time in time intervals used for calculating MPI (b). And, we concluded that this was resulted from decreased myocardial mass due to myocardial injury secondary to preeclampsia-related hypoxia.

According to the results of the study, elongation in right and left ventricle MPI was detected to be more significant compared to systolic and diastolic functions for determining preeclampsia-related cardiac injury in newborns of preeclamptic mothers within 24–48 hours of their life. Ventricle functions of the newborns of preeclamptic mothers should also be evaluated with MPI measurement besides conventional echocardiographic measurements.

Study limitation

Cardiac enzyme (CK, CK-MB, troponin I) measurements could also be included in the study to show subclinical myocardial injury which was shown with prolonged MPI in study group. However, it was not included in the study as drawing blood is an invasive intervention.

Disclosure statement

No potential conflict of interest was reported by the authors.

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